REMARKS

Summary of Interview

Applicants thank Examiners Chandra and Caputa for the courtesy extended to their agent, Melissa Kolom, during a telephonic interview held on March 15, 2005. The matters discussed during the interview are substantially as set forth herein.

The Invention

The present invention provides a compound of SEQ ID NO: 1, which compound binds an Src homology 2 (SH2) domain in a protein comprising an SH2 domain, is non-phosphorylated, and has a turn conformation upon binding to Grb2.

The Pending Claims

Upon entry of this amendment, claims 1, 5, 6, 9, and 23 will be pending. Claim 1 is directed to the above-described compound. Claims 5 and 6 are directed to a conjugate comprising the compound and a carrier agent. Claims 9 and 23 are directed to a composition comprising the compound and the conjugate, respectively.

Amendments to the Claims

Claim 1 has been amended to delete language relating to *in vivo* redox stability and IC_{50} concentration of the claimed compound. Claim 9 has been amended to delete languate relating tothe conjugate, which , which language has been incorporated into new claim 23. Claim 2 has been cancelled. Applicants reserve the right to pursue any canceled subject matter in a continuation, continuation-in-part, divisional, or other application. Cancellation of any subject matter should not be construed as abandonment of that subject matter. Accordingly, no new matter has been added by way of the amendments to the claims.

The Office Action

Claims 1, 2, 5, 8-11, 17, 25-27, 36, 37, 39, 50, 51, 53, 77, and 78 are rejected under 35 § U.S.C. 112, first paragraph, for an alleged lack of enablement. Applicants note that claims 2, 8, 10, 11, 17, 25-27, 36, 37, 39, 50, 51, 53, 77, and 78 are not pending in the subject application. Indeed, prior to this amendment, the current application has never contained more than 22 claims. Thus, the claims set forth in the Office Action as being subject to the enablement rejection are incorrect. As the only claims currently pending are claims 1, 5, 6, 9, and 23, the non-enablement rejection is considered to apply to these claims.

Discussion of Rejection Under 35 U.S.C. § 112, First Paragraph

The Office Action contends that claims 1, 5, 6, and 9, which are directed to a particular compound, as well as a conjugate and a composition comprising the compound, are not enabled by the subject application. The Office Action acknowledges that the specification adequately discloses how to make the claimed compound, conjugate, and composition (Office Action at p. 3), but alleges that the specification does not provide any guidance to one of ordinary skill in the art as to how to use the compound of SEQ ID NO: 1 to prevent breast cancer. Although the pending claims do not recite a method for treating cancer, the Office Action alleges that the treatment of breast cancer is the only disclosed utility of the claimed peptide, and predicates the Section 112, first paragraph, rejection on the alleged failure to enable the disclosed utility.

A. The Patent Office Has Failed to Establish a Prima Facie Case

The Applicants' stated utility is presumed to be correct. *In re Brana*, 51 F.3d. 1560, 1566, 34 U.S.P.Q. 2d. 1436, 1441 (Fed. Cir. 1995). As such, the PTO has the initial burden of challenging the presumptively correct assertion of utility. *Id.* Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such person of the invention's asserted utility. *Id.*

The present specification discloses that the claimed compound can be used, for example, to treat breast cancer. The Patent Office has provided no evidence that one of ordinary skill in the art would reasonably doubt the asserted utility. The Patent Office has not, for instance, come forward with evidence that questions the anti-cancer properties of the claimed compound. Instead, the Patent Office argues only that *in vitro* data, such as the data presented in the Applicant's specification, is a poor indicator of therapeutic efficacy in a human. In support of this argument, the Patent Office presents several journal articles that pertain to compounds that are different from the claimed compound, which references allegedly suggest that *in vitro* and even *in vivo* data are not accurate predictors of therapeutic potential. As such, the Patent Office attempts to place the burden on the Applicants to prove the stated utility. However, the Applicants are not required to do so under the law.

The Federal Circuit held in *In re Brana* that a *prima facie* case of non-enablement with respect to an applicant's stated utility of an anti-cancer compound was not established by evidence that merely challenged the predictive value of a particular testing model. *Id.* In *Brana*, the application under consideration claimed certain anti-tumor compounds, and stated that the claimed compounds were more effective than related prior art compounds, which

were disclosed in the prior art as having *in vivo* efficacy in animal models. *Id.* at 1562-63, 34 U.S.P.Q. 2d. at 1438. The Board of Patent Appeals and Interferences affirmed a rejection of the claims under Section 112, first paragraph, as allegedly failing to enable the disclosed utility because the prior art *in vivo* animal model data of the related compounds was not a good predictor of the utility of the claimed compounds in humans. *Id.* at 1563-64, 34 U.S.P.Q. 2d. at 1439.

The Federal Circuit reversed the Board decision, holding that the Patent Office failed to satisfy its initial burden of challenging the presumptively correct assertion of utility, and that the specification of *Brana* satisfied section 112 and the statutory utility requirement. *Id.* at 1566-68, 34 U.S.P.Q. 2d. at 1441-43. In particular, the Federal Circuit stated:

> The references cited by the Board ... do not question the usefulness of any compound as an antitumor agent or provide any other evidence to cause one of skill in the art to question the asserted utility of applicants' compounds. Rather these references merely discuss the therapeutic predictive value of *in vivo* murine tests – relevant only if the applicants must prove the ultimate value in humans of their asserted utility.

Id. at 1566, 34 U.S.P.Q. 2d. at 1441. The Federal Circuit further stated that "the purpose of treating cancer with chemical compounds does not suggest an inherently unbelievable undertaking or involve implausible scientific principles" and that the Patent Office's proffered evidence challenging the predictive value of *in vivo* testing does not provide a sufficient basis to doubt the stated utility. *Id.*

In the present case, the Patent Office has presented evidence that challenges only the predictive nature of testing models, generally, and has not provided any evidence that raises doubt as to the stated utility of the claimed compound as an anti-cancer agent. Accordingly, under *Brana*, the Patent Office has not met its burden of establishing a *prima facie* case for non-enablement, and the burden of proof does not shift to the Applicants to prove their stated utility. For this reason alone, the rejection of the pending claims is improper and should be withdrawn.

B. The Evidence Presented in the Present Application is Sufficient to Establish the Usefulness of the Claimed Compound as an Anti-Cancer Agent

Even if the Patent Office could meet its burden of proof by its submission of evidence challenging the predictive nature of *in vitro* testing, which it cannot, the evidence supplied in the background section of the application, which strongly suggests the therapeutic value of inhibitors of SH2 domain binding, in combination with the disclosure of the invention as a

whole is sufficient to overcome the evidence proffered by the Patent Office. In this regard, the Applicants emphasize that they are claiming a compound, not a method of treating cancer in a human, and they are not required to prove the efficacy of the compound as an anti-cancer agent in a human. As the Federal Circuit stated in *Brana*:

> The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas, such as the treatment of cancer.

Id. at 1568, 34 U.S.P.Q. 2d. at 1442-43. Thus, the evidence provided in the present application itself is sufficient to establish the utility of the claimed compounds as anti-cancer agents even in view of the Patent Office's arguments.

For this additional reason, the Section 112 rejection is improper and should be withdrawn.

C. The Patent Office Has Not Considered Additional Disclosed Utilities

The present application discloses uses of the claimed compound other than for the treatment of cancer, which uses the Patent Office has ignored. For instance, the claimed compound is disclosed to be effective for inhibiting cell proliferation via inhibition of SH2 protein domain binding (see, e.g., page 2, lines 7-9, and page 7, lines 17-18), and the inhibition of MAP kinase activation, which is a known cell signaling molecule implicated in various cancers (see, e.g., Reddy et al., *Cancer Metastasis Rev.*, 22(4), 395-403 (2003)) (see Example 10). It is readily apparent to one of ordinary skill in the art that the claimed compound with the above properties has substantial uses other than for the treatment of cancer, such as for researching conditions associated with cell proliferation and aberrant cell signaling (see, e.g., Kurogi, *Med Res. Rev., 23*(1):15-31 (2003)).

These additional stated utilities are enabled by the present application, and the Section 112 rejection is improper and should be withdrawn for this additional reason.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

John L. Gase, Reg. No. 47,590
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
180 North Stetson Avenue
Chicago, Illinois 60601-6780
(312) 616-5600 (telephone)
(312) 616-5700 (facsimile)

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